regions, so that the recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions, wherein said recombinant adenovirus genome additionally contains a transgene that replaces any one of said deletions.

38. (twice amended) A replication-defective recombinant adenovirus, wherein the virus contains at least two lethal deletions, two lethal mutations, or one lethal deletion and one lethal mutation in the E1 and E4 early gene regions, wherein an essential region of the E4 early gene region is deleted or mutated, so that the recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions, and wherein said recombinant adenovirus genome additionally contains a transgene that replaces any one of said deletions.

39. (twice amended) A packaging cell line derived from a 293 cell that supports the growth of a replication defective recombinant adenovirus that carries at least two lethal deletions of adenovirus E1 and E4 early gene regions, so that the recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions, comprising a cell line that supplies the function of the E1 early region and the E4 early region operably linked to an inducible promoter and virus-associated RNA sequences.

40. (amended) A DNA plasmid comprising an inducible promoter operably linked to nucleotide sequences encoding a cytotoxic gene product of an adenoviral E4 gene or E4 early gene region.

41. The DNA plasmid of Claim 40 wherein said inducible promoter is the promoter from the cAMP response element binding protein regulated genes.

42. The DNA plasmid of Claim 41 wherein said inducible promoter is selected from the gene encoding mammalian alpha inhibin.

43. The DNA plasmid of Claim 41 wherein said inducible promoter is selected from the gene encoding mouse alpha inhibin.

44. The DNA plasmid of Claim 41 wherein said inducible promoter is selected from the gene encoding the tetracycline ~~responsive promoter.~~

45. The plasmid pIK6.1 MIP(α)-E4 designated ATCC #75879.

46. (twice amended) A recombinant adenoviral vector, wherein said vector comprises at least two lethal deletions, two lethal mutations or one lethal deletion or one lethal mutation selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and additionally comprises a transgene that replaces any one of said deletions

so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions[, and additionally may comprises a transgene that replaces any one of said deletions].

47. (twice amended) A recombinant adenoviral vector comprising at least two lethal deletions in the E1 and E4 early gene regions, and a transgene that replaces any one of said deletions so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions[, and optionally a deletion of the E3 gene region, and a transgene that replaces any one of said deletions].

48. (twice amended) A packaging cell line derived from a 293-cell that supplies the function of the E4 early region operably linked to an inducible promoter and that supports the growth of a mutant adenovirus defective in replication, wherein said adenovirus comprises at least two lethal deletions, at least two lethal mutations, or at least one lethal mutation and one lethal deletion selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and [optionally a deletion of the E3 gene region], so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

49. (twice amended) A packaging cell line derived from a 293 cell that supplies the function of the E4 early region operably linked to an inducible promoter and that supports the growth of a recombinant adenoviral vector comprising a transgene, wherein said vector comprises at least two lethal deletions, two lethal mutations or one lethal deletion and one lethal mutation selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes[, and optionally a deletion of the E3 gene region], so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

50. (twice amended) A packaging cell line derived from a 293 cell that supplies the function of the E4 early region operably linked to an inducible promoter and that supports the growth of an adenoviral vector, wherein said vector comprises at least lethal two deletions selected from the group consisting of E1 and E4 early gene regions and a transgene that replaces any one of said deletions [and optionally a deletion of the E3 gene region], so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

DJ Cont

Cancel Claim 51.

52. The replication-defective recombinant adenovirus of Claim 38 in which the region of the E4 early gene region which is deleted or mutated is open reading frame 6.

NE